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PATENT
Attorney Docket No. 0147-0199P

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS:	KUFER, P. et al.	CONF.:3425
SERIAL NO.:	09/554,465	GROUP: 1641
FILED:	May 12, 2000	EXAMINER: CHEU, C.

FOR: A NOVEL METHOD OF IDENTIFYING BINDING SITE DOMAINS THAT RETAIN THE CAPACITY OF BINDING TO AN EPITOPE

RESPONSE TO RESTRICTION REQUIREMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

April 4, 2003

Sir:

In response to the Examiner's Office Action dated December 4, 2002, the period for response having been extended four (4) months to April 4, 2003, the following remarks are respectfully submitted in connection with the above-identified application.

The Examiner has required a restriction between the claims of Groups I – IV as follows:

Group I:	claims 1-20 drawn to a method of identifying a binding site domain having capacity of binding to a predetermined epitope in a recombinant bi or multivalent polypeptide in a phage display system;
Group II:	claims 21, 22-24 and 27-29 drawn to polypeptide product;
Group III:	claims 21, 22-24 and 27-29 drawn to antibody products comprising binding sites of fusion proteins; and

Group IV: claims 25-26 drawn to polynucleotides encoding the said antibodies or polypeptides and cells transfected with the said polynucleotides.

The Examiner argues that the restriction requirement is proper because the invention(s) are not so linked as to form a single general inventive concept under PCT Rule 13.1. This requirement is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Applicants submit that the Examiner has not properly construed or applied the unity of invention standard applicable under PCT Rule 13, as is clear from a review of the international phase of this application. Since this is the national phase of a PCT application, unity of invention must be analyzed under PCT Rule 13. The Examiner will note that no unity of invention objection was raised during the international phase of this application, which applied the unity of invention standard of PCT Rule 13. An international application which complies with those unity of invention requirements must then be accepted by all of the designated and elected offices, including the USPTO, since Article 27(1) of the Patent Cooperation Treaty does not permit any national law or national office to require compliance with different regulations relating to the contents of the international application. Thus the U.S. application must be examined for Unity of Invention consistent with the Patent Cooperation Treaty, not just by giving verbal assent to the unity of invention standard by mere reference to the PCT Rule, but rather an actual application of the standard. See *Caterpillar Tractor Co. v. Commissioner of Patents and Trademarks*, 231 USPQ 590 (E.D. VA 1986). In this case, proper application of the unity of invention standard means that the application of PCT Rule 13 by the USPTO should be consistent with the application by the PCT Examiner of the same rule for the same subject matter. This means that the Examiner's restriction requirement is improper, in that all of the claims in the application should be searched and examined together.

Furthermore, Applicants offer the following comments in response to the Examiner's comments on pages 2-3 of the Office Action regarding common concept linking the claims in the present application. Applicants would like to point out that, in the method of the invention, the bi-specific polypeptide comprises one "surrogate" specificity. Basically, this surrogate specificity may be changed into a different specificity without simultaneously losing the binding

specificity of the non-surrogate molecule. *McGuinness et al.*, in contrast, select for the binding specificities of the bi-specific heterodimeric diabody directly. In other words, the binding specificities in *McGuinness et al.* within the bi-specific molecule are selected for as such and no subsequent modification of the molecule is envisioned whereas in the present invention, the surrogate domain may be exchanged for a different binding specificity. Moreover, it should be noted that *McGuinness et al.* only describes diabodies that can directly be expressed and selected for in *E. Coli* (by phage display). The present invention, however, allows molecules that cannot be functionally expressed in *E. Coli*. In accordance with the invention, the surrogate molecule allows expression in *E. Coli* and the subsequent replacement of the surrogate molecule by a different binding specificity will form the final construct. It should be noted that this final construct will, in accordance with the invention, also retain the binding specificity of the molecule that was originally selected for in *E. Coli* when expressed with this new binding partner and when expressed in eukaryotic cells. Thus, it is not seen how the Examiner can properly assert that the present claims are not novel in view of *McGuinness et al.*

In view of the foregoing remarks, Applicants submit that all of the claims of Groups I-IV (i.e. claims 1-29) form a single general inventive concept under PCT Rule 13.1 and should be examiner together in a single application.

However, in order to be fully responsive to the Office Action, if the Examiner maintains the full scope of the restriction requirement, then Applicants provisionally elect to prosecute the claims of Group I, i.e. claims 1-20.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned below at 714-708-8555 in Costa Mesa, CA to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), the Applicant respectfully petitions for a four (4) month extension of time for filing a response in connection with the present application and the required fee of $725.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail, postage prepaid, in an envelope to: Commissioner of Patents and Trademarks, Washington D.C. 20231 on: April 4 2003
(Date of deposit)

BIRCH, STEWART, KOLASCH & BIRCH, LLP

Lori M. Jill
(Signature)

April 4 2003
(Date of Signature)